Neoplastic Proliferations of White Cells

(Myeloid Neoplasms)

- from hematopoietic progenitors
- Primarily involve
  - -bone marrow
  - &replace normal marrow elements
- Lesser secondary (Rarely metastasized to other site)
  - Hematopoietic organs
    - -LN
    - -spleen
    - -liver

Three broad categories

Acute myeloid leukemia

blocked at an early stage(immature) of development

↓

Immature myeloid cells (blasts) accumulate in BM & frequently circulate in PB

Not always

(مش ضروري عشان اسميه leukemia
يكون عندي خلايا في BP)

Myeloproliferative neoplasms

neoplastic clone continues to terminal differentiation (They reach the end stage)
but with ↴
increased or dysregulated growth

Myelodysplastic syndromes

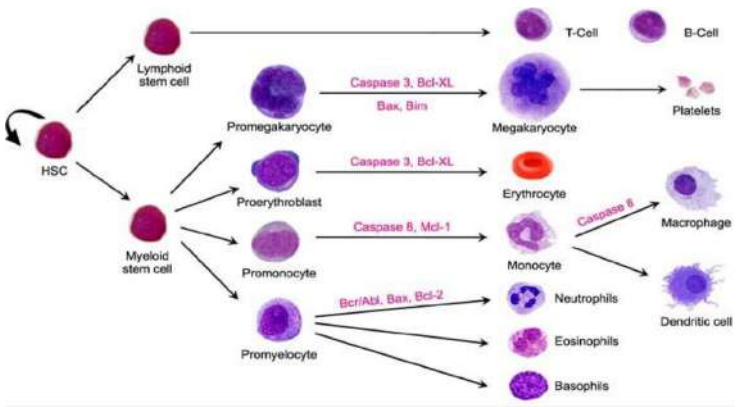
terminal differentiation occurs but in a disordered and ineffective fashion

↓

dysplastic BM precursors & PB cytopenias.

Dysplasia function & morphology

Chronic leukemia	VS	Acute leukemia
▷ Mature cells		▷ Blasts
▷ Gradual proliferation.		▷ Rapid proliferation .
▷ More indolent (2-6 years without Tx)		▷ Rapidly Fatal (<6 months without Tx)
▷ Lymphoid ... CLL		▷ Lymphoid..ALL
▷ MPN... CML		▷ Myeloid ... AML



Acute myeloid leukemia (AML)

Done by: Saja Al-raggad

Acute myeloid leukemia (AML)

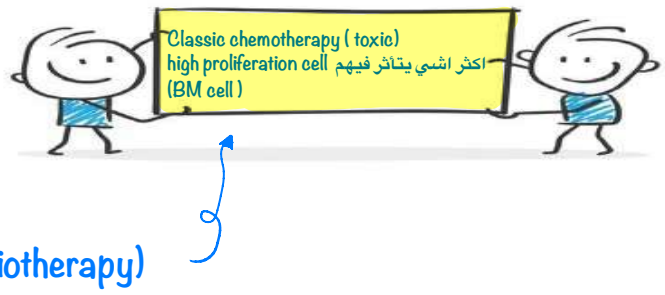
*Acute

*all age group, peak > 60 years ← ممكن أشوفها ب young إذا في
Risk factor or genetic predisposition

*Clinical signs & symptoms
[anemia, thrombocytopenia, neutropenia] → from the replacement of normal marrow elements by leukemic blasts

*Splenomegaly & lymphadenopathy & brain involvement are less prominent than in ALL

Risk factors



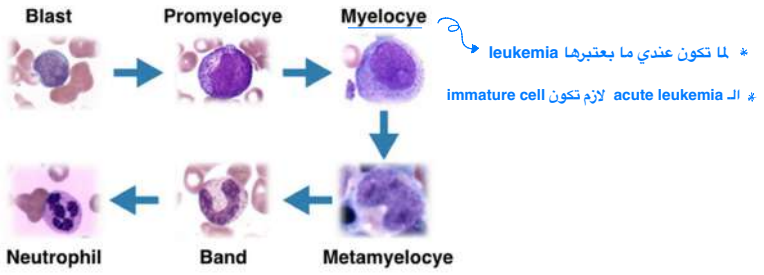
- Increase age.
- Male sex
- Previous cancer treatment. (Therapy related like radiotherapy)
- Exposure to radiation (survivors of a nuclear reactor accident).
- Dangerous chemical exposure (benzene)
- Smoking; cigarette smoke (contains benzene & other chemicals)
- Other blood disorders (MDS, MPN)
- Genetic disorders (Down syndrome) ← Risk for 2 leukemia : 1-ALL 2-AML(بعمر صغير)

Pathogenesis

*mutations in genes encoding transcription factors that are required for normal myeloid cell differentiation → interfere with the differentiation of early myeloid cells → accumulation of myeloid precursors (blasts) in BM.

the best prognosis
curable in > 90%

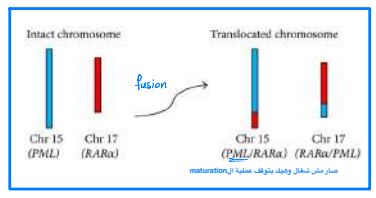
in acute promyelocytic Leukemia (APL)



* لما تكون عندي ما بعتبرها leukemia
* الـ acute leukemia لازم تكون immature cell

fusion of retinoic acid receptor a (RARA) gene on chr. 17 & PML gene on chr. 15 → PML/RARA fusion protein → blocks myeloid differentiation at promyelocytic stage.

صورة للتوضيح :



ATRA

highly effective therapy

(analogue of vitamin A)

*overcomes this block → induce the neoplastic promyelocytes to differentiate into neutrophils rapidly → clears the tumor

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Classification

AMLs are very diverse in terms of
-genetics
-cellular lineage
-degree of maturation

(1) **AMLs ass with specific genetic aberrations**: important coz they predict outcome & they guide therapy. Like t(15;17)

(2) **AMLs with dysplasia**: arise from MDSs.

(3) **AMLs occurring after genotoxic chemotherapy.**

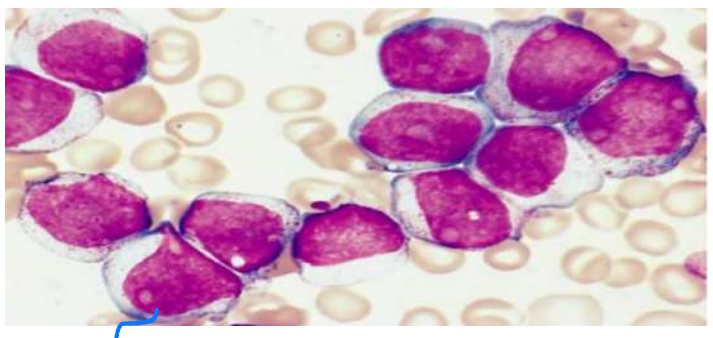
(4) **AMLs, Not otherwise specified**: subclassified based on the predominant line of differentiation

Class	Prognosis
I. AML With Recurrent Chromosomal Translocations	
AML with t(8;21)(q22;q22); *RUNXT1/RUNX1* fusion gene	Favorable
AML with inv(16)(p13;q22); *CBFB/MYH11* fusion gene	Favorable
AML with t(15;17)(q22;q21.1); *PML/RARA* fusion gene	Favorable

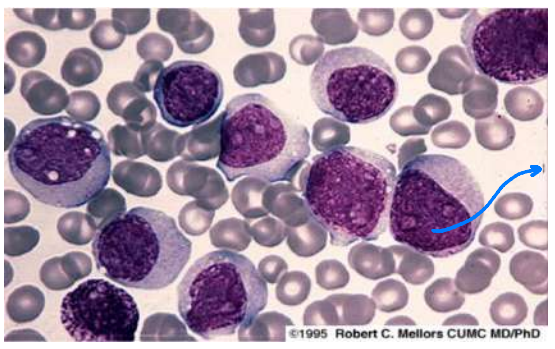
Morphology

* the presence of at least 20% myeloid blasts or promyelocytes of BM cellularity

-Normal count blast cell →(1٪)
-(20٪) or more →leukemia



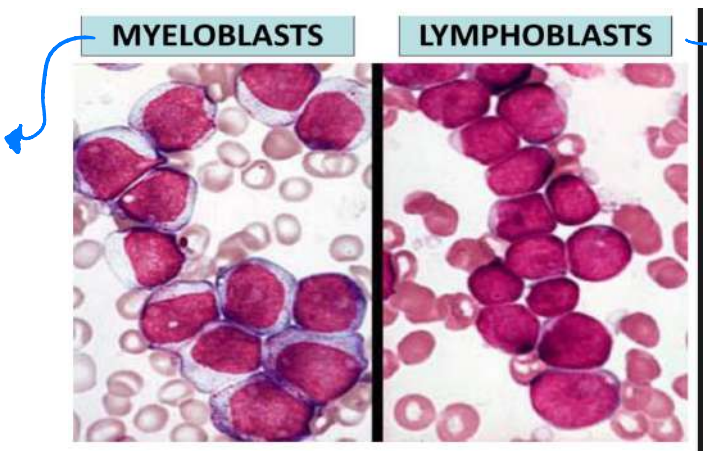
-Large cells
-Large nucleus
-Prominent nucleolus
-Good amount of cytoplasm
-Azurephilic granules



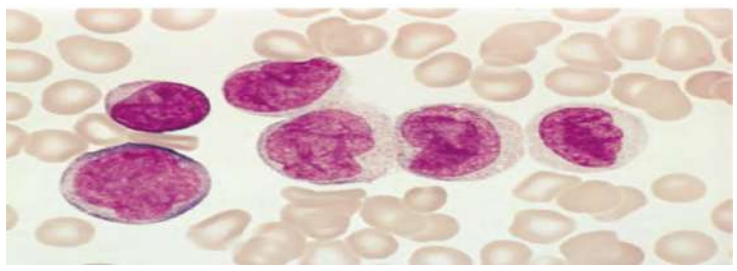
تغييرات في سطح النوية نفسها

* Indentation or irregularity in cytoplasm
* Prominent nuclei :
(ما رح تكون زي ←Hodgkin lymphoma)

* delicate nuclear chromatin
* 2-4 nucleoli
* larger cytoplasm than lymphoblasts
* fine azurophilic cytoplasmic granules.

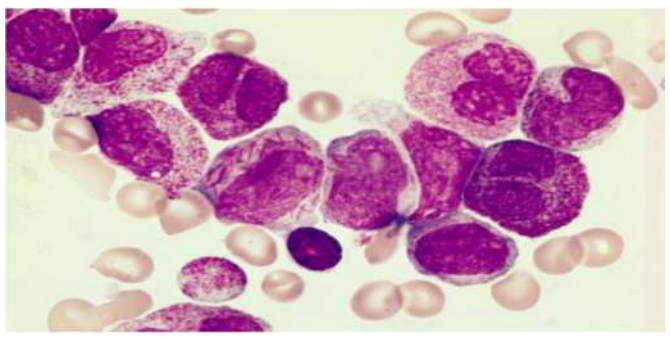


الخلية أغلبها nucleus
وكمية قليلة من cytoplasm
ما في (prominent nuclei)

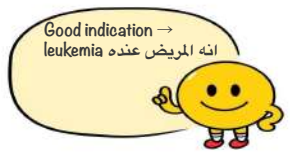


Monoblasts:
have folded or lobulated nuclei, lack Auer rods.
Kidney -shape

لانها تابعة لل M3



Auer rods :
(Myeloperoxidase exists inside azurophilic granules)



red-staining needle-like azurophilic granules
Numerous in acute promyelocytic leukemia

من الأساس موجودين بس صار فيهم cristalization

(aleukemic leukemia) → In other subtypes of AML, 1. monoblasts, 2. erythroblasts or 3. megakaryoblasts predominate.

blasts are entirely absent from PB

↓ For this reason

BM examination is essential to exclude acute leukemia in pancytopenic patients
(ال blast بكونوا في BM)

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Immunophenotype (heterogeneous)

* Most tumors express some combination of myeloid-associated antigens; CD13, CD14, CD15, or CD117 (KIT).

* CD34: a marker of hematopoietic stem cells & present on myeloblasts.

* Myeloperoxidase (MPO) (most specific) → Lysosomal enzyme : Monocyte مش موجود في

Esterase enzyme (monocyte)

Clinical features

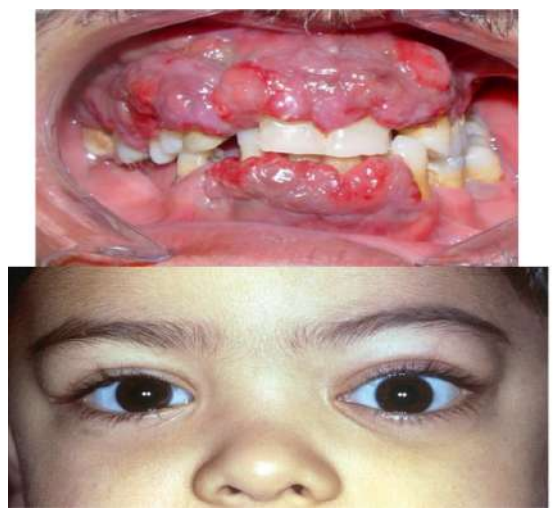
* within weeks or a few months

* Symptoms :
  1.anemia 2. neutropenia 3.thrombocytopenia 4. pancytopenia

* CNS manifestations → less frequent than ALL.

* Procoagulants and fibrinolytic factors → high DIC incidence (t (15:17) غالباً مع لكن ممكن يجي مع اي نوع)

* Tumors with monocytic differentiation
  - (leukemia cutis)
  - gingiva



* localized soft-tissue mass
  - myeloblastoma
  - granulocytic sarcoma (هي فعليا مش (sarcoma) ← مش من bone)

Prognosis

* devastating disease

* good-risk" karyotypic abnormalities (t[8;21], inv[16]) are associated with a 50% chance of long-term disease-free survival (قلب — In the same chromosome)

* Overall survival in all patients is only 15-30% with conventional chemotherapy

(Bad prognosis)

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